Novel Therapeutic Approaches in Nasopharynx Cancer

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Professor Anthony Chan obtained his MBBS in University College London and completed his postgraduate training in UK before joining the Chinese University of Hong Kong in 1993. He was appointed Chairman of the Department of Clinical Oncology in July 2002. He is currently the Chief of Service of Department of Clinical Oncology; as well as the Director of the Hong Kong Cancer Institute and Sir YK Pao Centre for Cancer. His research has focused on the clinical and translational research of Asian cancers. His group has undertaken pivotol phase III studies and developed novel therapeutic strategies in nasopharynx cancer.

Intensity-modulated radiotherapy achieves local control rates of over 90% and is increasingly regarded as the standard radiation technique for nasopharynx cancer (NPC). Concurrent cisplatin-radiotherapy given either as weekly or 3 weekly schedule with or without adjuvant cisplatin-5FU has emerged as the standard therapy for patients presenting with locoregionally advanced disease. The current generation of randomized studies aims to address the additive benefit of neoadjuvant chemotherapy particularly using newer and less toxic agents including taxanes and gemcitabine. With encouraging results of concurrent C225-radiotherapy in head and neck cancers and clinical benefit demonstrated using carboplatin and C225 in metastatic NPC, the next generation of studies will include the use of agents targeting the EGFR receptor in locoregionally advanced NPC. In metastatic NPC, ongoing studies are undertaken using non-platinum combination aimed at reducing toxicities, as well as the efficacy of targeted agents such as Iressa. A pilot study using Azacitidine in treatment-refractory locally recurrent NPC patients demonstrated for the first time the successful demethylation of latent and lytic Epstein-Barr virus promoters in post-treatment NP biopsies, achieving pharmacologic reversal of dense CpG methylation in tumor tissue. In this study, treatment with Azacitidine alone did not activate viral antigen expression, and a follow-up study adding a histone deacetylase inhibitor will be conducted to further pursue the therapeutic potential of treatment targeted at reactivating the expression of epigenetically silenced genes in NPC.

Tumour-derived cell-free EBV DNA has been consistently detected in NPC patients, and using a real-time quantitiative PCR technique, EBV DNA has a diagnostic sensitivity of 96% and specificity of 93%. Our group has shown that pretreatment EBV DNA levels correlated with disease stage and that it was a highly significant prognosticator for treatment outcome and survival. EBV DNA is a useful tool for monitoring patients during radiotherapy and chemotherapy, as well as for early detection of tumour recurrence. A persistently raised EBV DNA level at 6-8 weeks after radiotherapy completion was significantly associated with poorer overall survival compared with patients with low or undetectable EBV DNA levels. Further studies are being undertaken to investigate the use of this marker in risk-stratification of patients for treatment.